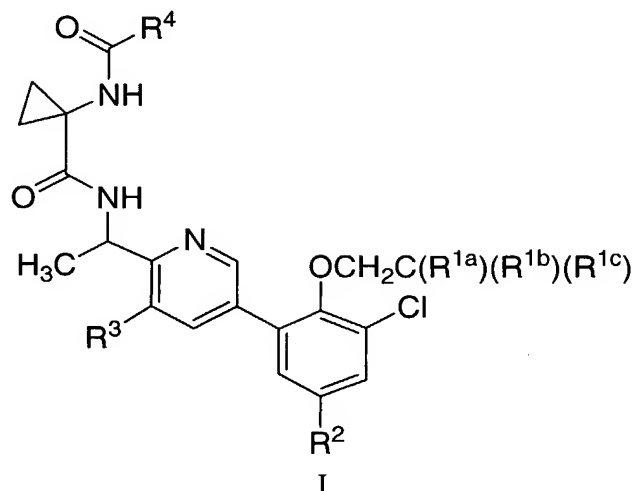


WHAT IS CLAIMED IS:

1. A compound of formula I and pharmaceutically acceptable salts thereof:



wherein

R^{1a}, R^{1b} and R^{1c} are each independently selected from hydrogen and fluorine;

10 R² is hydrogen or chlorine;

R³ is chlorine or fluorine; and

R⁴ is selected from (1) C₁₋₆ alkyl optionally substituted with 1 to 3 groups independently selected from halogen, nitro, cyano, OR^a, SR^a, COR^a, SO₂R^d, CO₂R^a, OC(O)R^a, NR^bR^c, NR^bC(O)R^a, NR^bC(O)₂R^a, C(O)NR^bR^c, and C₃₋₈ cycloalkyl, (2) C₃₋₈ cycloalkyl optionally substituted with 1 to 3

15 groups independently selected from halogen, nitro, cyano and phenyl, (3) aryl optionally substituted with 1 to 3 groups independently selected from halogen, nitro, cyano, OR^a, SR^a, C(O)₂R^a, C₁₋₄ alkyl and C₁₋₃ haloalkyl, wherein aryl is selected from phenyl, 3,4-methylenedioxyphenyl and naphthyl, and (5)

heterocycle optionally substituted with 1 to 3 groups independently selected from halogen, nitro, cyano, OR^a, SR^a, C₁₋₄ alkyl optionally substituted with OR^a, C₃₋₆cycloalkyl, phenyl and C₁₋₃ haloalkyl

20 wherein said heterocycle is selected from (a) a 5-membered heteroaromatic ring having a ring heteroatom selected from N, O and S, and optionally having up to 3 additional ring nitrogen atoms; (b) a 6-membered heteroaromatic ring containing from 1 to 3 ring nitrogen atoms and N-oxides thereof; and (c) a 5- or 6-membered non-aromatic heterocyclic ring selected from tetrahydrofuranyl, 5-oxotetrahydrofuranyl, 2-oxo-2H-pyran, 2-pyrrolidinone, and 6-oxo-1,6-dihydropyridazinyl;

25 R^a is selected from (1) hydrogen, (2) C₁₋₄ alkyl optionally substituted with 1 to 5 halogen atoms, (3) phenyl optionally substituted with 1 to 3 groups independently selected from halogen, cyano, nitro, OH,

C₁₋₄ alkyloxy, C₃₋₆ cycloalkyl and C₁₋₄ alkyl optionally substituted with 1 to 5 halogen atoms, (4) C₃₋₆ cycloalkyl, and (5) pyridyl;

R^b and R^c are independently selected from (1) hydrogen, (2) C₁₋₄ alkyl optionally substituted with 1 to 5 groups independently selected from halogen, amino, mono-C₁₋₄alkylamino, di-C₁₋₄alkylamino, and

- 5 SO₂R^d, (3) (CH₂)_k-phenyl optionally substituted with 1 to 3 groups selected from halogen, cyano, nitro, OH, C₁₋₄ alkyloxy, C₃₋₆ cycloalkyl and C₁₋₄ alkyl optionally substituted with 1 to 5 halogen atoms, and (4) C₃₋₆ cycloalkyl, or

R^b and R^c together with the nitrogen atom to which they are attached form a 4-, 5-, or 6-membered ring optionally containing an additional heteroatom selected from N, O, and S; or

- 10 R^b and R^c together with the nitrogen atom to which they are attached form a cyclic imide;
R^d is selected from (1) C₁₋₄ alkyl optionally substituted with 1 to 3 halogen atoms, (2) C₁₋₄ alkyloxy, and (3) phenyl optionally substituted with 1 to 3 groups selected from halogen, cyano, nitro, OH, C₁₋₄ alkyloxy, C₃₋₆ cycloalkyl and C₁₋₄ alkyl optionally substituted with 1 to 5 halogen atoms; and
k is 0, 1 or 2;

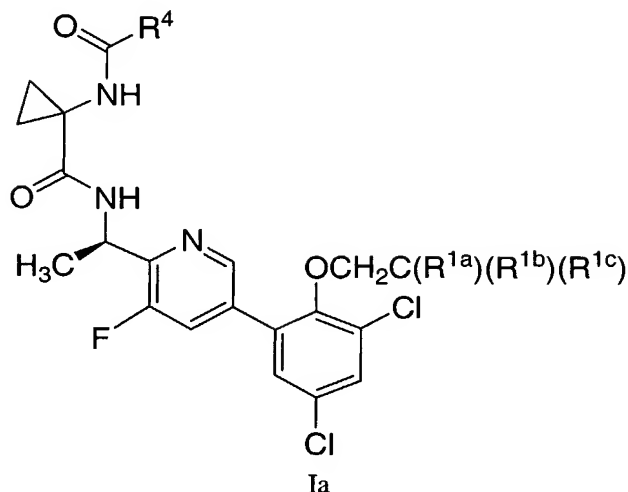
- 15 with the proviso that when R⁴ is trifluoromethyl or unsubstituted isoxazolyl, R³ is fluorine.

2. A compound of Claim 1 wherein C(R^{1a})(R^{1b})(R^{1c}) is selected from CH₃, CF₂H and CF₃.

- 20 3. A compound of Claim 1 wherein R⁴ is an optionally substituted 5-membered heteroaromatic ring having a ring heteroatom selected from N, O and S, and optionally having up to 3 additional ring nitrogen atoms, wherein said substituent is 1 to 2 groups independently selected from halogen, OR^a, C₁₋₄ alkyl optionally substituted with OR^a, C₃₋₆cycloalkyl, phenyl and C₁₋₃ haloalkyl.

- 25 4. A compound of Claim 1 wherein R⁴ is an optionally substituted 6-membered heteroaromatic ring containing from 1 to 3 ring nitrogen atoms and N-oxides thereof, wherein said substituent is 1 to 2 groups independently selected from halogen and C₁₋₄ alkyl.

5. A compound of Claim 1 having the formula Ia and pharmaceutically acceptable salts thereof:



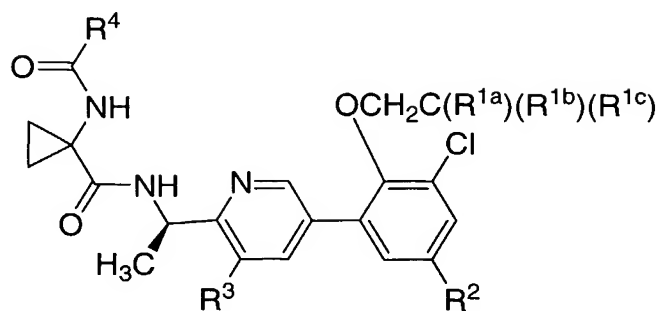
wherein R^{1a}, R^{1b} and R^{1c} are each independently selected from hydrogen and fluorine;

R⁴ is (a) optionally substituted 5-membered heteroaromatic ring having a ring heteroatom selected from N, O and S, and optionally having up to 3 additional ring nitrogen atoms; or (b) optionally substituted 6-membered heteroaromatic ring containing from 1 to 3 ring nitrogen atoms and N-oxides thereof; wherein the substituent is 1 to 2 groups independently selected from halogen, C₁₋₄alkyl optionally substituted with C₁₋₄alkoxy, C₁₋₄alkoxy, hydroxy, C₃₋₆ cycloalkyl, and CF₃.

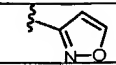
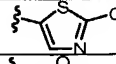
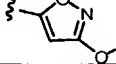
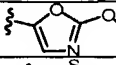
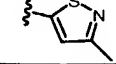
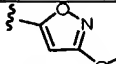
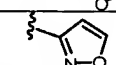
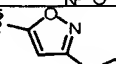
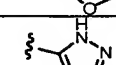
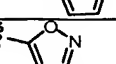
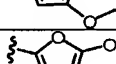
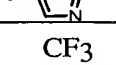
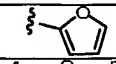
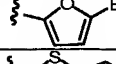
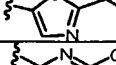
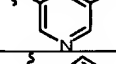
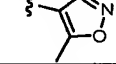
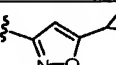
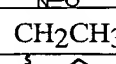
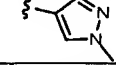
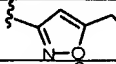
6. A compound of Claim 5 wherein R⁴ is selected from optionally substituted isoxazolyl, optionally substituted oxazolyl, optionally substituted isothiazolyl, optionally substituted thiazolyl, optionally substituted pyridazinyl and optionally substituted pyrazinyl, wherein the substituent is 1 to 2 groups selected from halogen, C₁₋₄alkyl optionally substituted with C₁₋₄alkoxy, C₁₋₄alkoxy, hydroxy, and CF₃.

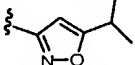
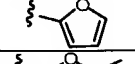
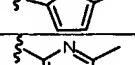
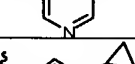
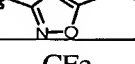
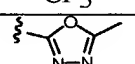
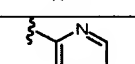
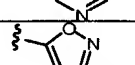
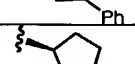
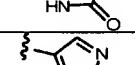
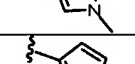
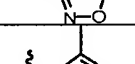
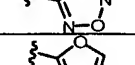
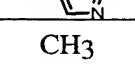
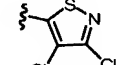
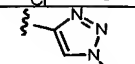
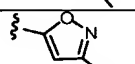
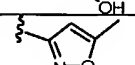
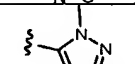
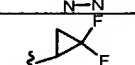
7. A compound of Claim 5 wherein R⁴ is selected from 3-chloro-5-isoxazolyl, 3-methoxy-5-isoxazolyl, 3-ethoxy-5-isoxazolyl, and 3-methyl-5-isoxazolyl.

















8. A compound of Claim 1 selected from:










R ⁴	C(R ^{1a})(R ^{1b})(R ^{1c})	R ²	R ³
	CF ₂ H	Cl	F
	CF ₂ H	Cl	F
	CF ₂ H	Cl	F
	CF ₂ H	Cl	F
	CF ₂ H	Cl	F
	CF ₂ H	Cl	F
	CH ₃	Cl	F
	CF ₂ H	Cl	F
CH ₃	CF ₂ H	Cl	F
	CF ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
CH ₂ CN	CH ₃	CH	F
	CH ₃	Cl	F
	CF ₂ H	Cl	F
	CH ₃	Cl	F

R ⁴	C(R ^{1a})(R ^{1b})(R ^{1c})	R ²	R ³
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	Cl
	CH ₃	Cl	F
	CH ₃	Cl	F
	CF ₂ H	Cl	Cl
	CH ₃	Cl	Cl
	CF ₂ H	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
CF ₃	CF ₂ H	H	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
CH ₂ CH ₃	CH ₃	Cl	F
	CF ₂ H	Cl	F
	CF ₂ H	Cl	F
	CH ₃	Cl	F
CH ₂ SO ₂ CH ₃	CF ₂ H	Cl	F
	CH ₃	Cl	F

R4	C(R1a)(R1b)(R1c)	R2	R3
	CF ₂ H	Cl	F
	CF ₂ H	Cl	F
	CF ₂ H	Cl	F
	CH ₃	Cl	F
	CF ₂ H	Cl	F
CF ₃	CH ₃	H	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CF ₂ H	Cl	F
	CF ₂ H	Cl	F
	CH ₃	Cl	F
	CF ₃	Cl	Cl
	CF ₂ H	Cl	F
	CH ₃	Cl	F
CH ₃	CH ₃	Cl	F
	CH ₃	Cl	F
	CF ₂ H	Cl	F
	CF ₂ H	Cl	F
	CF ₂ H	Cl	Cl
	CH ₃	Cl	F
	CF ₃	Cl	F
	CH ₃	Cl	F

R ⁴	C(R ^{1a})(R ^{1b})(R ^{1c})	R ²	R ³
	CH ₃	Cl	Cl
	CH ₃	Cl	F
CClF ₂	CH ₃	Cl	F
	CF ₃	Cl	Cl
(CH ₂) ₂ CH ₃	CH ₃	Cl	F
CH(CH ₃) ₂	CH ₃	Cl	F
	CF ₂ H	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
CHF ₂	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F

R ⁴	C(R ^{1a})(R ^{1b})(R ^{1c})	R ²	R ³
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CF ₂ H	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F
	CH ₃	Cl	F

and pharmaceutically acceptable salts thereof.

9. A pharmaceutical composition which comprises a therapeutically effective amount of a compound of Claim 1 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

10. Use of a compound of Claim 1 or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of conditions mediated by bradykinin B₁ receptor.